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Commentary

Additional Notes on the Case-Control Study in Western Washington on the Cancer Risk from Asbestos in Drinking Water

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It is important to note that my presentation was a summary of our work and that a paper with a fuller description of procedures and detailed tables and risk estimates will be published in another journal (*1*).

One questioner asked what factors determined "no exposure" and what proportions of the cases and controls had no exposure? For each place of residence or work, the following factors could have led to an absence of exposure to Sultan River drinking water: (1) the place was located outside the boundaries of the Sultan River distribution system; (2) the place was located inside the boundaries of the Sultan River distribution system at a time when the Sultan River was not on line as a source of water for that area; (3) a subject worked at a job that, though based in the Sultan River area, involved extensive travel away from the place of employment; and (4) the subject did not use a community water supply, as water was obtained from a well, bottle or other sources. There was no estimated exposure to asbestos in drinking water in 1% of the cases and 0.6% of the controls.

The asbestos concentration in the drinking water from the Sultan River was specifically measured. Twenty-two samples were taken from the distribution system from June 1978 to April 1979. There was quite a large seasonal variation in concentration. After correction for seasonal variation, we found that the concentrations varied only randomly across the Sultan River area. The average of all uncorrected concentrations was used as the reference exposure value for work or residence episodes in the Sultan River area. A similar procedure was applied to the 73 water samples from other water sources outside the Sultan River area. The methods used for measuring asbestos concentrations are described in our companion paper. We also determined fiber length; 86% of the fibers were less than 1 μm in length.

Concerning the sensitivity of the study, we were asked why the similarity of estimated exposures of cases and controls did not reduce the power to detect risks. The similarity of estimated exposures between cases and controls appears to be a consequence of the low true relative risks involved. A null finding in any epidemiologic study would manifest itself in the form of similar exposures between cases and controls. If there are true, but small differences in exposure, a much larger study would be needed to detect them.

It is important to consider that the main difference between our study and an ecologic study is the manner in which exposures were assigned to subjects. We obtained a detailed history of the residence and work location of each subject. We also asked each subject about typical water intake and use of bottled water, wells, and other water sources. Water company officials supplied us with a complete history of the Sultan River and other local water distribution systems. The result of this is that for any given date in a subject's history we could determine the level of exposure to asbestos in drinking water. The exposures were accumulated across each subject's lifetime and were, thus, highly specific per subject. In an ecologic study, all subjects residing in a specific area would have been assigned the same exposure, regardless of residence and work history and personal consumption habits.

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We would like to respond to questions about control selection. We randomly chose living, unmatched general population controls. The sampling frame was developed by using 1970 census maps with household counts updated from recent aerial photographs. A more complete description of the controls and comparison of the quality of the data from living and deceased subjects will be available in our companion paper (*1*). We found that the accuracy of responses to key questions was similar between living cases (53% of the cases were alive at interview), next of kin of deceased cases, and controls.

We were asked why certain positive results were dismissed because of a lack of similar results for the opposite sex. The questioner asked us to consider known sex differentials in susceptibility to cancer, exposure to asbestos, and exposure to cocarcinogens. The sex-inconsistent risk for stomach and pharyngeal cancer was only one of the factors that made us conservative in our interpretation. The 95% confidence intervals for the relative risks for male pharynx and stomach cancers also approached 1.0. In addition, since many significance tests were performed in the study, the multiple comparisons problem must also be considered when reviewing results. Based on these criteria, we feel that the results for male pharyngeal and stomach cancers are not strong enough to suggest a causal relationship between these cancers and imbibed asbestos. The best course would be to include these sites in additional studies that might be carried out.

One questioner suggested that the number of cases and controls for most of the individual sites were probably too few and that it was implied in the presentation that the power was inadequate for certain sites of importance, such as the stomach and pancreas. The questioner further noted that by dismissing the apparent significant risks found for male stomach, male pharynx, and female pancreas cancers there was the implication that there was some inherent bias or lack of ability to control for confounding factors in the study. We definitely had low power to detect risks of interest for several of the sites we studied. Obviously, we cannot say anything firm about the negative results for these sites. The statistically significant results for pharynx and stomach cancers are not inconsistent with this. Low power to obtain significant results does not mean that such results will not occur, since a chance mechanism is at work. The relative risks for female pancreas ranged from 1.4 to 1.7, depending on the analysis. The smallest significance level was 0.07. The relative risks for male pancreas were less than 1.0. The bottom line is that we do not know the reason for the elevated risks for male pharynx and stomach cancers. A case-control study cannot include every possible risk factor. For most cancer sites the risk attributable to known factors is a small fraction of the total risk. Hence, in any study, unknown and uncontrolled risk factors could give spurious results due to correlation with a specific risk factor in question. The problem is inherent in the investigator's partial knowledge of nature and not in our study design.

Finally, one questioner asked us to provide a short, simple description of the statistical procedure used. Our main procedure, logistic regression, is similar to the multiple regression procedure that is commonly used in many branches of science. In ordinary multiple regression one is predicting, for example, weight from height and other factors. In our logistic regression we are estimate the probability that a subject is a cancer case (versus population control) using asbestos-in-water exposure and other risk factors. In the regression procedure a risk factor that is associated with cancer would lead to a large estimated probability that a subject who had that factor was a case rather than a control. The logistic regression procedure is highly flexible and can, for example, be used in an analysis that is similar to the Mantel-Haenszel pooled odds ratio.

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REFERENCE

1. Polissar, L., Severson, R. K., and Boatman, E. S. A case control study of asbestos in drinking water and cancer risk. Am. J. Epidemiol., in press.